

Amendments to the Specification:

Please amend the specification as follows:

(I) Page 1, lines 4-19: please delete the paragraphs and substitute therefore with following paragraphs:

“The subject of the present invention is a new stable formulation in the form of sustained-release microgranules containing ~~Gingko Bileba~~ Ginkgo biloba extract as well as the process for preparing it.

More precisely, the present invention relates to microgranules in the form of a core containing ~~Gingko Bileba~~ Ginkgo biloba extract with at least one pharmaceutically acceptable excipient, an intermediate layer coating said core, and an outer layer, which enables sustained release of ~~Gingko Bileba~~ Ginkgo biloba from the core.

~~Gingko Bileba~~ Ginkgo biloba extract contains flavone glycosides (flavonoids), such as quercetin, kaemferol, isorhamnetin and terpenes (heterosides) such as Bilobadide, ginkgolide A, ginkgolide B, ginkgolide C, ginkgolide J.”

(II) Page 2 lines 4- 22: please delete the paragraphs and substitute therefore with following paragraphs:

“The multiparticulate form of the invention makes it possible to obtain a stable and reproducible sustained release multiparticulate dosage form comprising ~~Gingko Bileba~~ Ginkgo biloba extract, with the advantage of being stable during storage, particularly in accelerated storage conditions, defined in ICH as 40°C for temperature and 75% for relative humidity.

According to the present invention, the sustained release microgranules contain a ~~Gingko Bileba~~ Ginkgo biloba extract, characterized by the release of total flavone glycosides having the following profile of dissolution rates, measured at 37. 0°C ± 0. 5°C, with a Dissolution Test Apparatus I (Basket method at 100 rpm, 900 mL of purified water, W Detection : 272 nm) :”

(III) Page 3 lines 2- 17: please delete the paragraphs and substitute therefore with following paragraphs:

“These granules containing ~~Gingko Bileba~~ Ginkgo biloba extract are further characterized in that they comprise :

- a neutral core coated with a layer containing ~~Gingko Bileba~~ Ginkgo biloba extract, with at least one pharmaceutically acceptable excipient,
- an optionnal water-repellent layer, coating said core, comprising at least a polymer or a thermoplastic excipient,
- an outer polymeric layer which sustain the release of said extract from the active core.

~~Gingko Bileba~~ Ginkgo biloba extract may be in a concentrated preparation which are liquid, solid or of intermediate consistency, generally obtained from dried plant raw materials, preferably leaves, or in a powder form.”

(IV) Page 4 lines 12- 28: please delete the paragraphs and substitute therefore with following paragraphs:

“~~Gingko Bileba~~ Ginkgo biloba extracts contain up to 40% by weight of flavonoids, and up 10% by weight of terpenes.

Preferred ~~Gingko Bileba~~ Ginkgo biloba extracts contain 24% by weight of flavonoids and 6% by weight of terpenes.

The neutral core consists of a substance chosen from sugar, starch, mannitol, sorbitol, xylitol, cellulose, talc and mixtures thereof.

The neutral core may also consist of a starch/sucrose core in 80/20 mass ratios which is coated with 80% by weight of starch. In such neutral cores, the proportion by mass of sugar is advantageously less than 20%.

The layer containing the ~~Gingko Bileba~~ Ginkgo biloba extract contains at least one pharmaceutically acceptable excipient, selected from the group comprising a binder, an antistatic agent or a lubricant, preferably a binder.”

(V) Page 5 lines 5- 7: please delete the paragraph and substitute therefore with following paragraph:

“The binder is used in proportions of at most about 50%, preferably at most 20% by weight of ~~Gingko Bileba~~ Ginkgo biloba extract.”

(VI) Page 5 lines 25- 30: please delete the paragraph and substitute therefore with following paragraph:

“In order to prevent sticking between granules, mainly due to ~~Gingko Bileba~~ Ginkgo biloba extract, it is necessary to optionally apply an intermediate layer between the active layer comprising the ~~Gingko Bileba~~ Ginkgo biloba extract and the polymeric layer ensuring sustained release of said extract.”

(VII) Page 7 lines 1- 6: please delete the paragraph and substitute therefore with following paragraph:

“The plasticizer is selected in the group consisting of dibutyl sebacate triacetine, triethylacetate, triethylcitrate, ethylphtalate, or mixtures thereof. The plasticizer is used in proportions of at most about 30%, preferably 10% by weight of the ~~coating polymers~~ coating agents.”

(VIII) Page 8 lines 15- 28: please delete the paragraph and substitute therefore with following paragraph:

“The process for the preparation of sustained- release microgranules containing ~~Gingko Bileba~~ Ginkgo biloba extract comprises the successive steps consisting in:

- Applying over a neutral core, a layer comprising ~~Gingko Bileba~~ Ginkgo biloba extract, and at least one pharmaceutical excipient, preferably a binder.
- Coating said core with an intermediate layer over the thus obtained granules by spraying thereon a suspension, or a solution comprising a polymer or a thermoplastic excipient

- Coating the thus coated granules with an outer layer by spraying a suspension, a dispersion or a solution of a sustained-release coating composition,
- Drying the thus obtained coated granules.”

(IX) Page 9 lines 8- 13: please delete the paragraph and substitute therefore with following paragraph:

“According to the process of the invention, the cores are obtained by powder-coating, advantageously carried out by alternately spraying an alcoholic or aqueous-alcoholic solution comprising at least one pharmaceutical excipient, preferably a binder, and the ~~Gingko Bileba~~ Ginkgo biloba extract.”

(X) Page 10 lines 3- 5: please delete the paragraph and substitute therefore with following paragraph:

“This method was developed in order to detect release of total flavone glycosides from microgranules containing ~~Gingko Bileba~~ Ginkgo biloba extract.”

(XI) Page 10 lines 19- 23: please delete the paragraph and substitute therefore with following paragraph:

“This method was developed in order to assay total flavone glycosides content from microgranules containing ~~Gingko Bileba~~ Ginkgo biloba extract, and specifically assay quercetin, kaemfortol and isohamnetin content from granules.”

(XII) Page 11 lines 4- 8: please delete the paragraph and substitute therefore with following paragraph:

“84 grams of neutral cores are placed in a coating-pan, A 10% (w/w) binding solution of shellac, dissolved in isopropyl alcohol is prepared, then sprayed over neutral core as ~~Gingko Bileba~~ Ginkgo biloba extract is gradually added at the same time.

(XIII) Page 13 lines 5- 8: please delete the paragraph and substitute therefore with following paragraph:

“A 10% (w/w) binding solution of PVP K30, dissolved in isopropyl alcohol is prepared, then sprayed over neutral core as ~~Gingko Bileoba~~ Ginkgo biloba extract is gradually added at the same time.”

(XIV) Page 14 lines 7- 9: please delete the paragraph and substitute therefore with following paragraph:

“Sustained release microgranules comprising ~~Gingko Bileoba~~ Ginkgo biloba are prepared according the process of example to example 2 (see table 5).”

(XV) Page 15 lines 1- 4: please delete the paragraph and substitute therefore with following paragraph:

“Microgranules thus obtained are encapsulated in hard-gelatin capsules, each containing 120 mg of ~~Gingko Bileoba~~ Ginkgo biloba extract, said capsules being packed in PVC/Alu blisters.”